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10/565,616	06/09/2006	Zee Upton	FAK8011	2998
26294	7590	10/11/2011		
TAROLLI, SUNDHEIM, COVELL & TUMMINO L.L.P. 1300 EAST NINTH STREET, SUITE 1700 CLEVELAND, OH 44114			EXAMINER	
			SGAGIAS, MAGDALENE K	
		ART UNIT	PAPER NUMBER	
		1632		
		MAIL DATE	DELIVERY MODE	
		10/11/2011	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/565,616	Applicant(s) UPTON ET AL.
	Examiner MAGDALENE SGAGIAS	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 07 June 2011.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.
- 4) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 5) Claim(s) 1-6, 8-28, 35-37 is/are pending in the application.
- 5a) Of the above claim(s) 3,4,6,8-20,24-28,35 and 36 is/are withdrawn from consideration.
- 6) Claim(s) _____ is/are allowed.
- 7) Claim(s) 1,2,5,21-23 and 37 is/are rejected.
- 8) Claim(s) _____ is/are objected to.
- 9) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 10) The specification is objected to by the Examiner.
- 11) The drawing(s) filed on 01/24/2006 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 12) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08)
 Paper No(s)/Mail Date _____
- 4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date _____
- 5) Notice of Informal Patent Application
- 6) Other: _____

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 06/07/2011 has been entered.

Applicant's arguments filed 06/07/2011 have been fully considered. The amendments to the claims dated 06/07/2011 have been entered. Claims 1-6, 8-28, 35-37 are pending. Claims 7, 29-34, 38 are canceled. Claims 3-4, 6, 8-20, 24-28, 35-36 are withdrawn. Claims 1-2, 5, 21-23, and 37 are under consideration.

Claim Objections

Claims 1 and 23 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, claim 1 recites "VN fragment comprising amino acid residues 1-52 of mature VN", while depended claim 23 recites a broader range of: "wherein said vitronectin (VN).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 5, 21-23, and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the phrase "amino acid residues 1-52 of mature VN". It is not clear whether the amino acid sequences 1-52 of mature VN will be the same the amino acid sequences 1-52 of mature VN in all animal species. The recitation of specific amino acid residues is relative to where the start of a peptide is, and can contain allelic variations even within a species.

Claims 2, 5, 21-23, and 37 depend from claim 1.

Claim Rejections - 35 USC § 112

The rejection of claims **1-2, 5, 21-23, 37** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment dated to claim 1 in steps (i)(a) and (ii), where an IGFBP not present in an IGF-II/VN synthetic chimera is not required.

To the extent the claimed compositions are not described in the instant disclosure, claims **1-2, 5, 21-23, 37** are also rejected under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendment to claim 1 in steps (i)(a) and (ii) where an IGFBP not present in an IGF-II/VN synthetic chimera is not required.

Claim Rejections - 35 USC § 112/New Matter

The rejection of claims **1-2, 5, 21-23, 37** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment dated 06/07/2011, where an IGFBP not present in an IGF-II/VN synthetic chimera is not required.

To the extent the claimed compositions are not described in the instant disclosure, claims **1-2, 5, 21-23, 37** are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since the applicants disclosure do not teach a composition that is adequately described in the specification is withdrawn in view of the amendment dated 06/07/2011, where an IGFBP not present in an IGF-II/VN synthetic chimera is not required.

Claim Rejections - 35 USC § 112

The rejection of claims **1-2, 5, 21-23, 37** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of the amendment dated 06/07/2011, where an α_1 integrin-receptor binding vitronecin (VN) fragment comprising amino acid residues 1-52 of mature VN.

Claims **2, 5, 21-23, and 37** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims functional amino acid sequences 1-52 of mature VN and insulin-like growth factor. The claims read on a broad genus of sequences.

The written description requirement for a genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicants were in possession of the claimed invention. In the instant case, the specification does not sufficiently describe a representative number of functional mutants of vitronectin of amino acid sequences 1-52 of mature vitronectin from different species by actual reduction to practice or by disclosure of relevant identifying characteristics.

Applicant claim a functional amino acid sequences 1-52 of mature VN and insulin-like growth factor by function only, without any disclosed or known correlation between the elements and their function. The specification does not teach how to make all variable sequences of all animal species of amino acid sequences 1-52 of mature VN and insulin-like growth factor and still have it function to an α_v integrin-receptor binding vitronectin. The BLAST sequence alignment among the various species of amino acid sequences 1-52 of mature VN shows that there is no 100% homology among the various species (See Blast alignment below). Furthermore, the numbering of amino acids depends upon the start of the peptide, which can differ between species or have allelic variations within the same species.

The skilled artisan cannot envision a sufficient number of embodiments of the instant invention from the instant specification because the specification does not disclose amino acid sequences 1-52 of mature VN and insulin-like growth factor.

The state of the art at the time of filing does not provide sufficient information on the subject to overcome the deficiencies of the instant specification. There is no description in the

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art that allows one to envision a representative number of functional amino acid sequences that comprise amino acids 1-52 of mature VN and insulin-like growth factor variable sequences by disclosing structural or functional features of the sequences that are encompassed by sequences that contain amino acid residues 1-52 of mature VN from any animal species and insulin-like growth factor so that one of skill in the art could envision the claimed invention. Thus the skilled artisan cannot consult the art at the time of filing to envision a sufficient number of embodiments of the instant invention to see that the applicant was in possession of the claimed genus.

Neither the specification of the instant application or the state of the art at the time of filing teaches a structure-function relationship for a representative number of functional variable of amino acid residues 1-52 of mature VN from any species and insulin-like growth factor. As a result, the skilled artisan would not be able to envision the claimed invention. Therefore applicant has not satisfied the written description requirement to show the skilled artisan that they were in possession of the claimed genus.

BLAST alignment: amino acid sequences 1-52 of mature VN.

>[pdb|1OC0|B](#) Chain B, Plasminogen Activator Inhibitor-1 Complex With Somatomedin B Domain of Vitronectin
[pdb|1S4G|A](#) Chain A, Somatomedin-B Domain Of Human Plasma Vitronectin.
[pdb|1SSU|A](#) Chain A, Structural And Biochemical Evidence For Disulfide Bond
Heterogeneity In Active Forms Of The Somatomedin B Domain
Of Human Vitronectin
Length=51

Score = 61.2 bits (147), Expect = 5e-15, Method: Compositional matrix adjust.
Identities = 27/33 (82%), Positives = 29/33 (88%), Gaps = 0/33 (0%)

Query 20	DQESCKGRCTQQFMASKKQCDELCTYYQSCKA	52
	DQESCKGRCT+GF	KKCQCDEL+CYYQSCK
Sbjct 1	DQESCKGRCTEGFNVDKKCQCDELCSYYYQSCKT	33

> [pdb|2JQ8|A](#) [S] Chain A, Solution Structure Of The Somatomedin B Domain From Vitronectin Produced In Pichia Pastoris Length=53

Score = 60.8 bits (146), Expect = 8e-15, Method: Compositional matrix adjust.
Identities = 27/33 (82%), Positives = 29/33 (88%), Gaps = 0/33 (0%)

Query 20 DQESCKGRCTQGFMASKKCQCDELCTYYQSCTA 52
DQESCKGRCT+GF KKCQCDEL+CYYQSCTC
Sbjct 1 DQESCKGRCTEGFNVDKKCQCDELCSYYQSCT 33

> [pdb|3BT1|B](#) [S] Chain B, Structure Of Urokinase Receptor, Urokinase And Vitronectin Complex Length=40

Score = 58.2 bits (139), Expect = 6e-14, Method: Compositional matrix adjust.
Identities = 26/32 (81%), Positives = 28/32 (88%), Gaps = 0/32 (0%)

Query 21 QESCKGRCTQGFMASKKCQCDELCTYYQSCTA 52
QESCKGRCT+GF KKCQCDEL+CYYQSCTC
Sbjct 1 QESCKGRCTEGFNVDKKCQCDELCSYYQSCT 32

> [pdb|3NKM|A](#) [S] Chain A, Crystal Structure Of Mouse Autotaxin
[pdb|3NKN|A](#) [S] Chain A, Crystal Structure Of Mouse Autotaxin In Complex With 14:0-Lpa
[pdb|3NKO|A](#) [S] Chain A, Crystal Structure Of Mouse Autotaxin In Complex With 16:0-Lpa
[pdb|3NKP|A](#) [S] Chain A, Crystal Structure Of Mouse Autotaxin In Complex With 18:1-Lpa
[pdb|3NKQ|A](#) [S] Chain A, Crystal Structure Of Mouse Autotaxin In Complex With 18:3-Lpa
[pdb|3NKR|A](#) [S] Chain A, Crystal Structure Of Mouse Autotaxin In Complex With 22:6-Lpa Length=831

Sort alignments for
this subject sequence by:

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<u>Percent identity</u>		<u>E value</u>	<u>Score</u>
<u>position</u>	<u>Subject start position</u>		<u>Query start</u>
Score = 37.0 bits (83), Expect = 1e-04, Method: Composition-based stats.			
Identities = 18/47 (38%), Positives = 25/47 (53%), Gaps = 3/47 (6%)			
Query 6 PFFILALVAWVSLADQESCKGRCTQ-GFMASKKCQCDELCTYYQSCC 51	P +L+ W + + SCKGRC + + C+C D LC Y SCC		
Sbjct 7 PPTVLSDSPWTNTSG--SCKGRCFELQEVGPPDCRCDNLCKSYSSCC 51			
 Score = 24.3 bits (51), Expect = 4.6, Method: Composition-based stats.			
Identities = 10/30 (33%), Positives = 11/30 (37%), Gaps = 0/30 (0%)			
Query 22 ESCKGRCTQGFMASKKCQCDELCTYYQSCC 51	E K RC + C C E C CC		
Sbjct 66 ECTKDRCGEVRNEENACHCSEDCLSRGDCC 95			

>` pdb|2XR9|A [] Chain A, Crystal Structure Of Autotaxin (Enpp2)
Length=827

Sort alignments for
this subject sequence by:

<u>Percent identity</u>		<u>E value</u>	<u>Score</u>
<u>position</u>	<u>Subject start position</u>		<u>Query start</u>
Score = 36.6 bits (83), Expect = 1e-04, Method: Composition-based stats.			
Identities = 18/47 (38%), Positives = 25/47 (53%), Gaps = 3/47 (6%)			
Query 6 PFFILALVAWVSLADQESCKGRCTQ-GFMASKKCQCDELCTYYQSCC 51	P +L+ W + + SCKGRC + + C+C D LC Y SCC		
Sbjct 7 PPTVLSDSPWTNTSG--SCKGRCFELQEVGPPDCRCDNLCKSYSSCC 51			
 Score = 24.3 bits (51), Expect = 4.9, Method: Composition-based stats.			
Identities = 10/30 (33%), Positives = 11/30 (37%), Gaps = 0/30 (0%)			
Query 22 ESCKGRCTQGFMASKKCQCDELCTYYQSCC 51	E K RC + C C E C CC		
Sbjct 66 ECTKDRCGEVRNEENACHCSEDCLSRGDCC 95			

>` pdb|2XRG|A [] Chain A, Crystal Structure Of Autotaxin (Enpp2) In Complex
With
The Ha155 Boronic Acid Inhibitor
Length=862

Sort alignments for
this subject sequence by:

Percent identity E value Score

position Subject start position Query start

Score = 36.6 bits (83), Expect = 2e-04, Method: Composition-based stats.
Identities = 18/47 (38%), Positives = 25/47 (53%), Gaps = 3/47 (6%)

Query 6 PPFILALVAWVSLADQESCKGRCTQ-GFMASKKCQCDELCTYYQSCC 51
P +L+ W + + SCKGRC + + C+CD LC Y SCC

Sbjct 42 PPTVLSDLSPWTNTSG--SCKGRCFELQEVGPPDCRCNLCKSYSSCC 86

Score = 23.9 bits (50), Expect = 5.2, Method: Composition-based stats.
Identities = 10/30 (33%), Positives = 11/30 (37%), Gaps = 0/30 (0%)

Query 22 ESCKGRCCTQGFMASKKCQCDELCTYYQSCC 51

E K RC + C C E C CC

Sbjct 101 ECTKDRCGEVRNEENACHCSEDCLSRGDCC 130

> pdb|2VSN|A [] Chain A, Structure And Topological Arrangement Of An O-GlcNAc

Transferase Homolog: Insight Into Molecular Control Of Intracellular Glycosylation

pdb|2VSN|B [] Chain B, Structure And Topological Arrangement Of An O-GlcNAc Transferase Homolog: Insight Into Molecular Control Of Intracellular Glycosylation

Length=568

Score = 25.4 bits (54), Expect = 1.6, Method: Composition-based stats.
Identities = 12/26 (46%), Positives = 15/26 (58%), Gaps = 0/26 (0%)

Query 12 LVAWVSLADQESCKGRCTQGFMASKK 37

VAV+ LAD E G T G MA ++

Sbjct 23 FVAWLMLDAELGMGDTTAGEMAVQR 48

> pdb|2VSY|A [] Chain A, Xanthomonas Campestris Putative Ogt (Xcc0866), Apostructure

pdb|2VSY|B [] Chain B, Xanthomonas Campestris Putative Ogt (Xcc0866), Apostructure

pdb|2JLB|A [] Chain A, Xanthomonas Campestris Putative Ogt (Xcc0866), Complex

With Udp-GlcNAc Phosphonate Analogue

7 more sequence titles

pdb|2JLB|B [] Chain B, Xanthomonas Campestris Putative Ogt (Xcc0866), Complex

With Udp-GlcNAc Phosphonate Analogue

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[pdb|2XGM|A](#) [S] Chain A, Substrate And Product Analogues As Human O-GlcNAc Transferase Inhibitors.
[pdb|2XGM|B](#) [S] Chain B, Substrate And Product Analogues As Human O-GlcNAc Transferase Inhibitors.
[pdb|2XGO|A](#) [S] Chain A, Xcogt In Complex With Udp-S-GlcNAc
[pdb|2XGO|B](#) [S] Chain B, Xcogt In Complex With Udp-S-GlcNAc
[pdb|2XGS|A](#) [S] Chain A, Xcogt In Complex With C-Udp
[pdb|2XGS|B](#) [S] Chain B, Xcogt In Complex With C-Udp
Length=568

Score = 25.4 bits (54), Expect = 1.6, Method: Composition-based stats.
Identities = 12/26 (46%), Positives = 15/26 (58%), Gaps = 0/26 (0%)

Query 12 LVAWVSLADQESCKGRCTQGFMASKK 37
VAW+ LAD E G T G MA ++
Sbjct 23 FVAWLMLADAELGMGDTTAGEMAVQR 48

>[pdb|1KEA|A](#) [S] [C] Chain A, Structure Of A Thermostable Thymine-Dna Glycosylase
Length=221

GENE ID: 3355209_pFV1_p10 | hypothetical protein
[Methanothermobacter thermautotrophicus] (10 or fewer PubMed links)

Score = 23.9 bits (50), Expect = 6.0, Method: Composition-based stats.
Identities = 7/15 (47%), Positives = 11/15 (73%), Gaps = 0/15 (0%)

Query 36 KKQCQCDELCTYYQSC 50
+KC +LC+YY+ C
Sbjct 205 EKCGMSKLCSYYEKC 219

>[pdb|2AI0|L](#) [S] Chain L, Anti-Cocaine Antibody 7.5.21, Crystal Form Iii
[pdb|2AI0|M](#) [S] Chain M, Anti-Cocaine Antibody 7.5.21, Crystal Form Iii
[pdb|2AI0|N](#) [S] Chain N, Anti-Cocaine Antibody 7.5.21, Crystal Form Iii
[pdb|2AI0|O](#) [S] Chain O, Anti-Cocaine Antibody 7.5.21, Crystal Form Iii
Length=217

Score = 23.5 bits (49), Expect = 6.8, Method: Composition-based stats.
Identities = 10/20 (50%), Positives = 12/20 (60%), Gaps = 0/20 (0%)

Query 16 VSLADQESCKGRCTQGFMAS 35
VSL DQ S RC+Q + S
Sbjct 13 VSLGDQASISCRCSQSIVKS 32

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> [pdb|2A1W|L] Chain L, Anti-Cocaine Antibody 7.5.21, Crystal Form I
[pdb|2A1W|M] Chain M, Anti-Cocaine Antibody 7.5.21, Crystal Form I
Length=216

Score = 23.5 bits (49), Expect = 7.4, Method: Composition-based stats.
Identities = 10/20 (50%), Positives = 12/20 (60%), Gaps = 0/20 (0%)

Query 16 VSLADQESCKGRCTQGFMAS 35
VSL DQ S RC+Q + S
Sbjct 13 VSLGDQASISCRCSQSIVKS 32

> [pdb|2A77|L] Chain L, Anti-Cocaine Antibody 7.5.21, Crystal Form II
Length=216

Score = 23.5 bits (49), Expect = 7.5, Method: Composition-based stats.
Identities = 10/20 (50%), Positives = 12/20 (60%), Gaps = 0/20 (0%)

Query 16 VSLADQESCKGRCTQGFMAS 35
VSL DQ S RC+Q + S
Sbjct 13 VSLGDQASISCRCSQSIVKS 32

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The rejection of claims 1-2 under 35 U.S.C. 102(b) as being anticipated by Upton et al [Endocrinology, 140(6): 2928-2931, 1999, (IDS) thereafter referred as Upton 1999] in view of Nagano et al [JBC, 267(34): 24863-24870, 1992] (IDS)]; Nakao et al (US 5,360,789; date issued; May 20, 1993); Schwartz et al (The International Journal of Biochemistry & Cell Biology

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31: 539-544, 1999); of Klemke et al, (The Journal of Cell Biology, 127: 859-866, 1994 (IDS)) is withdrawn in view of the amendment to the claims dated 06/07/2011.

Applicant's arguments are convincing in view of the amendment.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MAGDALENE K. SGAGIAS whose telephone number is (571)272-3305. The examiner can normally be reached on 8.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paras Peter can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Magdalene K. Sgagias,
Art Unit 1632

/Thaian N Ton/
Primary Examiner, Art Unit 1632